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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,632	02/25/2002	Timothy W. Starzl	4724-2	6303
22442	7590	12/13/2004	EXAMINER	
SHERIDAN ROSS PC 1560 BROADWAY SUITE 1200 DENVER, CO 80202			LUM, LEON YUN BON	
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			1641	

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/084,632	Applicant(s) STARZL ET AL.	
	Examiner Leon Y Lum	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 20-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 June 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>20041122</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of claims 1-19 in the reply filed on 19 October 2004 is acknowledged.

In the traverse, Applicants state that both the apparatus and method as claimed are not precluded from incorporating the feature of a compact disk, which is the feature that the Examiner used in the restriction of the apparatus claims from the method claims, and also state that both claimed inventions would require essentially the same prior art searching.

Applicants admit that both the apparatus and methods claims do not require use of a compact disk having digital images encoded thereon. Although Applicants contend that both the apparatus and method claims can incorporate a compact disk, MPEP § 806.05(e) clearly states that the inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. The process of reading encoded information on a compact disk is distinctly independent from the method as claimed, which requires a substance of interest present in a sample and is not the encoded digital information required for reading a compact disk. The claimed method also does not include any limitations that suggest encoded information on a compact disk. Since the claimed method does not

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include the limitations of a compact disk and the claimed apparatus is capable of practicing the distinct process of reading a compact disk, the restriction as made between claims 1-19 and 20-32 are maintained.

Drawings

2. The drawings were received on 19 June 2002. These drawings are not acceptable because amendments to drawings must include replacement sheets showing amended figures which include the desired changes without markings on a separate sheet for compliance with 37 CFR 1.84.

Specification

3. The preliminary amendment filed 19 June 2002 has been acknowledged and entered. However, the amendment to the specification is improper because it does not include markings to show changes. Markings in the specification must be included in amendments to show all changes relative to the immediate prior version.

4. The abstract of the disclosure is objected to because line 4 contains the legal phrase "herein" and line 5 contains the legal phrase "thereto". Correction is required. See MPEP § 608.01(b).

Claim Objections

5. Claim 16 is objected to because of the following informalities: the instant claim has two periods. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. In claim 1, line 3, the phrase "at least one of a setting and a position" is vague and indefinite. The specification does not define the phrase and it is unclear as to whether the limitation "at least one of" refers to both the setting and position embodiments, or to just one of the embodiments.

9. In claim 1, line 4, the phrase "making determinations" is vague and indefinite. The specification does not provide a definition for the phrase and it is unclear as to what the term "determinations" means. Does the instant phrase refer to making adjustments

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to the "instrument" (line 3), data analysis of the "substance of interest" (line 5), or adjustments to another step?

10. Claim 15 recites the limitation "at least one of integration time and gain associated with said light collection device" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

11. Claim 17 recites the limitations "said first subspot" and "said second subspot in lines 2-3 and 4, respectively. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

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3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-4, 8, 14, and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al (Biotechnic & Histochemistry, 1995, vol. 70, no. 4, pages 211-216) in view of Stimpson et al (US 5,599,668).

Gao et al reference teaches a method for analyzing a sample for binding events when a substance of interest is present with the sample, comprising establishing at least one of a setting and a position for an instrument that includes a control and that is involved with making determinations related to at least the presence of the substance of interest with the sample, positioning the sample relative to a light source that outputs a light beam, receiving said light beam by at least portions of the sample, collecting scattered light from the sample portions using a light collection device of said instrument, and processing digital image data based on said light collected during said

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collecting step using said control of said instrument, by disclosing the principle of epipolarization microscopy for the detection of a sample (Figures 1 and 5, and captions), wherein the detectable signal depends on the amount of adsorbed streptavidin-silver enhanced gold that gives off a certain intensity (page 215, left column, 1st full paragraph; and Figure 4 and caption).

However, Gao et al reference fails to teach the step of counting objects after said processing step using digital information in determining at least whether the substance of interest is present with the sample.

Stimpson et al reference discloses image processing of an assay for quantitative results to determine the level of binding pair members present in a fluid sample, wherein the image processing is performed on images of scattered light detected using a CCD (column 21, line 50 to column 22, line 65, especially column 21, lines 51-54 and column 22, lines 3, 20-22, 34-37, and 50-56), in order to detect one or more specific binding analytes, especially DNA or oligonucleotides, for sequencing purposes (column 1, lines 7-14 and column 3, lines 42-49).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Gao et al with the step of image processing of an assay for quantitative results to determine the level of binding pair members present in a fluid sample, wherein the image processing is performed on images of scattered light detected using a CCD, as taught by Stimpson et al, in order to detect one or more specific binding analytes, especially DNA or oligonucleotides, for sequencing purposes. One of ordinary skill in the art at the time of the invention would have reasonable

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expectation of success in including image processing to obtain quantitative results, as taught by Stimpson et al, in the method of Gao et al, since Gao et al teach light scatter detection using CCD devices, and the image processing taught by Stimpson et al is performed on scattered light detected by a CCD device.

With regards to claim 2, Gao et al reference teaches that said establishing step includes providing magnification related to collecting said scattered light, by disclosing that samples were evaluated using a 10 X objective lens (page 214, left column, 2nd paragraph, lines 1-6).

With regards to claims 3-4 and 8, Gao et al reference teaches that said establishing step includes locating an optical subsystem in a direction relative to the sample (claim 3), locating said light source such that said light beam is at a desired angle relative to the sample (claim 4), and that said processing step includes receiving electrical signals from said light collection device and obtaining said image data using said electrical signals (claim 8), by disclosing the tungsten light, filters, condenser, polarizer, dichrotic half-mirror, crossed-analyzer, diaphragm, mercury vapor lamp, CCD camera, and Image Processing Unit of an epipolarization microscopy, wherein the CCD camera is connected to the Image Processing Unit (Figure 5 and caption).

With regards to claim 14, Stimpson et al reference teaches the step of storing information in memory of said control related to said at least one of said setting and said position, by disclosing the digital information may be stored in RAM or any storage device for further manipulation (column 22, lines 20-22).

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With regards to claim 17, Stimpson et al reference teaches that the substance of interest is a first substance of interest and said image data from said first subspot includes information related to the first substance of interest when present and said second subspot has a second sample, different from the first sample, to be used in determining whether a second substance of interest, different from the first substance of interest, is present, by disclosing multiple capture sites on a support comprising a DNA array and collecting scattered light from each site, in order to measure binding of a light scattering label to simultaneously detect the presence of one or more specific binding analytes in a fluid sample through hybridization (column 3, lines 45-55 and 65-67; and column 4, lines 29-31).

With regards to claim 18, Gao et al reference teaches that said digital image is based on a two dimensional array of elements, by disclosing that the principle of epipolarization microscopy is performed with immunoassay on a microscope slide with 30 micro wells (page 211, left column, 1st paragraph to right column, 2nd paragraph).

With regards to claim 19, Gao et al reference teaches that the sample has a light-scattering label that includes colloidal gold, by disclosing colloidal gold conjugated to streptavidin that is immobilized to a biotin, which is bound to a secondary antibody that is attached to an antigen (Figure 1 and caption).

16. Claims 5, 9-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al (Biotechnic & Histochemistry, 1995, vol. 70, no. 4, pages

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211-216) in view of Stimpson et al (US 5,599,668) as applied to claim 1 above, and further in view of De Brabander (The Amer. J. Anat., 1989, vol. 185, pages 282-295).

Gao et al and Stimpson et al references have been disclosed above and Gao et al reference additionally teaches that said collection device includes a photoelectric device, by disclosing the CCD camera and Image Processing Unit, as stated above (Figure 5 and caption). However, Gao et al and Stimpson et al references fail to teach that said establishing step includes regulating a gain related to said photoelectric device to provide desired light contrast (claim 5) and adjusting a gain associated with said light collection device after conducting at least some of said processing step (claim 15).

De Brabander et al reference discloses the step of subtracting an equal amount of light from all pixels (increasing the offset) and expanding the remaining signal to the original value (increasing the gain), wherein a "mottle" image obtained with the preparation out of focus is stored in digital format in a frame memory and subtracted in real time from subsequent images, in order to produce an increase in intensity (contrast) to distinguish between gold particle markers and background signal, and increase the contrast of other elements that disturb the image, and to also improve visualization of contrast generated by the preparation itself (page 282, right column, 3rd paragraph to page 283, left column; and Figure 2 and caption).

It would have been obvious at the time of the invention to modify the method of Gao et al and Stimpson et al with the step of subtracting an equal amount of light from all pixels (increasing the offset) and expanding the remaining signal to the original value (increasing the gain), wherein a "mottle" image obtained with the preparation out of

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focus is stored in digital format in a frame memory and subtracted in real time from subsequent images, as taught by De Brabander, in order to produce an increase in intensity (contrast) to distinguish between gold particle markers and background signal, and increase the contrast of other elements that disturb the image, and to also improve visualization of contrast generated by the preparation itself. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in increasing the offset and gain of the image, as taught by De Brabander et al, in the method of Gao et al and Stimpson et al, since Gao et al and Stimpson et al teach image detection of light scattering from gold particles, and the image processing performed by De Brabander et al is conducted on images derived from gold particles.

With regards to claims 9-13, De Brabander et al reference teaches that said processing step includes using at least a first light intensity related procedure and at least a first size related procedure (claim 9), wherein said first light intensity related procedure includes performing a thresholding function related to light intensity (claim 10), said performing step includes using a histogram analysis (claim 11), wherein said first size related procedure includes filtering using at least one parameter related to size (claim 12), and said processing step includes providing a lower limit threshold based on histogram-related information (claim 13), by disclosing the step of first increasing the offset and then increasing the gain of pixels from an image, as stated above (page 282, right column, 3rd paragraph, lines 11-27; and Figure 2 and caption) wherein gold particles of 20-40 nm diameter provide sufficient contrast as individual units (page 284, left column, 1st paragraph), and a segmentation step based on pure gray-level

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information in a single pixel, wherein gold particles have significantly lower gray values than the background after 8-bit digitalization, and only gray levels lower than a certain threshold are retained to locate the gold pixels (page 286, right column, 4th paragraph to page 288, right column, last paragraph).

17. Claims 6-7 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al (Biotechnic & Histochemistry, 1995, vol. 70, no. 4, pages 211-216) in view of Stimpson et al (US 5,599,668) as applied to claim 1 above, and further in view of Oberhardt (US 6,251,615 B1).

Gao et al and Stimpson et al references have been disclosed above, but fail to teach that said light beam includes a laser beam and the sample is associated with a test spot and said establishing step includes having said laser beam encompass at least all of said test spot with uniform intensity (claim 6), said positioning step includes moving said light beam (claim 7), and the sample includes a test spot comprised of at least a first subspot and a second subspot immediately adjacent to said first subspot and in which said processing step includes obtaining said image data using said collection device from said first subspot, and separately obtaining said image data from said second subspot, and said counting step includes counting objects from said first subspot before obtaining said image data from said second subspot (claim 16).

Oberhardt reference teaches moving the microscope field from capture zone to capture zone on a surface, wherein a plurality of light sources, including epi-illumination and laser sources, provides illumination of the capture zones, and a CCD detector array

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connected to camera electronics and a computer images captured cells (column 25, lines 16-67, especially lines 16-28, 37-46, and 56-59; and Figure 12), and wherein as the microscope field moves systematically from section to section along the entire area of the upper surface of the chamber wall, a number of captured cells is counted such that a sequential interrogation is achieved and recorded (column 26, lines 19-22, 35-38, and 50-63), in order to provide a convenient analysis of samples containing suspended cells for research and clinical use, including measuring the kinetics of cell capture (column 2, lines 24-45).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Gao et al and Stimpson et al with the step of moving the microscope field from capture zone to capture zone on a surface, wherein a plurality of light sources, including epi-illumination and laser sources, provides illumination of the capture zones, and a CCD detector array connected to camera electronics and a computer images captured cells, and wherein as the microscope field moves systematically from section to section along the entire area of the upper surface of the chamber wall, a number of captured cells is counted such that a sequential interrogation is achieved and recorded, as taught by Oberhardt, in order to provide a convenient analysis of samples containing suspended cells for research and clinical use, including measuring the kinetics of cell capture. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in moving the microscope field, using a laser source, and sequentially counting bound analytes, as taught by Oberhardt, in the method of Gao et al and Stimpson et al, since Gao et al and Stimpson et al teach

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the detection of scattered light using a CCD camera and quantification of detected objects by post-image capture analysis using a computer, and the steps of Oberhardt include the detection of scattered light using a CCD camera and counting captured analytes using computer processing.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Leon Y Lum
Patent Examiner
Art Unit 1641



LYL



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

12/10/04